NEWS

Highres LC-MS/MS proteomics associated with dedicated bioinformatics/biostatistics is an efficient tool to show and understand the effects of drugs, actives, processes, disease…

For example, we studied cancer cells extracted from various points of a solid tumor by by LC-MS/MS proteomics (label-free untargeted relative quantification treated vs control) followed by CORAVALID™ analysis.

It showed metabolic changes on different scales and degrees, in effectors and regulators.

We were able to unravel the mechanisms underlying changes in interactions in the **extracellular matrix**, by examining interactors and protein domains. We also showed which biological and molecular processes showed signs of **dedifferentiation**, with down-regulation for proteins related to organelle organization; signal transduction and intercellular signalization; chromatine architecture maintenance, and regulation of DNA replication. Some among those were related to H3F3A histones dysregulation, which are known to be associated to diffuse and agressives tumors.
We also observed **signaling** mechanisms variations, with cell surface receptor linked signal transduction, antigen processing and presentation (linked to major histocompatibility complex), cell to cell signaling and cell communication, all being a staple of dedifferentiated cells. A particular emphasis was put on metabotropic glutamate receptor type I **pathways**, which thus could be involved in regulating signals modifying cell activity.
There was also metabolic differences, with some splicing anomalies which are also common in cancer cells (http://www.tau.ac.il/~gilast/PAPERS/cancer.pdf) ; but also related to energy and to nucleotide **metabolism** and **catalytic enzyme activities** (decreased transesterification, increased oxidoreduction). We were able to show that transcription alterations were not the main mechanism responsible for the change of proliferative state, but that it was more probably related to changes in signaling equipment (thus impairing cell regulations from the tissues and environment), **cell architecture and motion** proteins, which was extremely improved (cytoskeleton intermediate filaments proteins).
It was even possible to correlate these changes to the various specific **compartments** involved in the matter at work; and to **chromosomal expression distribution,** suggesting the etiology was related to **specific promoters,** and allowing the confirmation and distinction of **significant chromosomal alterations**, ie those related to a phenotype, among those observed through cytology **(*1p32-pter deletion*).**

The exhaustivity of the method allowed interpreting the results to objectively explain the phenomena in progress depending on the parameters of the experimental context, discriminating the changes between variants inside a same tissue depending on severity/grades distinction based on histological studies with the advantage of taking post-translational modifications and signaling pathway interplay into account. It revealed potential therapeutic targets and gave insights in mechanisms of proliferation and metastasis.

Results allow quick integrations of these into current researches, multiple metabolic pathways displays allowing additionally to replace the intervention level in the whole

picture of the assessed as pertinent mechanisms. They are also able to discriminate relationships invisible to human minds even given time using conventional studies.